FOOD AND DRUG ADMINISTRATION

CENTER FOR TOBACCO PRODUCTS

TOBACCO PRODUCTS SCIENTIFIC ADVISORY COMMITTEE (TPSAC)

Thursday, July 21, 2011

9:15 a.m. to 12:15 p.m.

Morning Session

9200 Corporate Boulevard

Rockville, Maryland

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P R O C E E D I N G S

(9:16 a.m.)

Call to Order

DR. SAMET: Good morning. I think we will go ahead and get started with our meeting. We're anticipating the arrival of one more committee member.

I'm Jon Samet, the chair of the Tobacco Products Scientific Advisory Committee. Good morning to everyone and thank you for joining us. I will note this reminds me of TPSAC meetings from a year ago when we were anticipating that a temperature record would be broken.

I wanted to make a few statements, then we'll introduce the committee.

For topics such as those being discussed at today's meeting, there are often a variety of opinions, some of which are quite strongly held. Our goal is that today's meeting will be a fair and open forum for discussion of these issues and that individuals can express their views without interruption. Thus, as a gentle reminder,

individuals will be allowed to speak into the record only if recognized by the chair. We look forward to a productive meeting.

In the spirit of the Federal Advisory Committee Act and the Government in the Sunshine Act, we ask that the advisory committee members take care that the conversations about the topics at hand take place in the open forum of the meeting. We are aware that members of the media are anxious to speak with the FDA about these proceedings. However, FDA will refrain from discussing the details of this meeting with the media until its conclusion.

Also, the committee is reminded to please refrain from discussing the meeting topics during breaks.

Thank you. And let me turn to Caryn Cohen for the conflict of interest statement.

Conflict of Interest Statement

MS. COHEN: The Food and Drug Administration is convening today's meeting of the Tobacco Products Scientific Advisory Committee under the

authority of the Federal Advisory Committee Act of 1972.

With the exception of the industry representatives, all members and non-voting members are special government employees or regular federal employees from other agencies and are subject to federal conflict of interest laws and regulations.

The following information on the status of this committee's compliance with federal ethics and conflict of interest laws, covered by, but not limited to, those found at 18 USC Section 208 and Section 712 of the Federal Food, Drug, and Cosmetic Act, is being provided to participants in today's meeting and to the public.

FDA has determined that members of this committee are in compliance with federal ethics and conflict of interest laws. Under 18 USC Section 208, Congress has authorized FDA to grant waivers to special government employees and regular federal employees who have potential financial conflicts when it is determined that the agency's need for a particular individual's services outweighs his or

her potential financial conflict of interest.

Under Section 712 of the FD&C Act, Congress has authorized FDA to grant waivers to special government employees and regular federal employees with potential conflicts of interest when necessary to afford the committee essential expertise.

Related to the discussion of today's meeting, members of this committee have been screened for potential financial conflicts of interest of their own, as well as those imputed to them, including those of their spouses or minor children, and, for purposes of 18 USC Section 208, their employers.

These interests may include investments, consulting, expert witness testimony, contracts, grants, CRADAs, teaching, speaking, writing, patents and royalties, and primary employment.

Today's agenda involves changes proposed by the committee members to the TPSAC monthly report submitted to the agency on March 18th, 2011.

This is a particular matters meeting during which general issues will be discussed. Based on

the agenda for today's meeting and all financial interests reported by committee members, no conflict of interest waivers have been issued in connection with this meeting. To ensure transparency, we encourage all committee members to disclose any public statements they have made concerning the issue before this committee meeting.

With respect to FDA's invited industry representatives, we would like to disclose that Drs. Daniel Heck and John Lauterbach and Mr. Arnold Hamm are participating in this meeting as non-voting industry representatives, acting on behalf of the interests of the tobacco manufacturing industry, the small business tobacco manufacturing industry, and tobacco growers, respectively.

Their role at this meeting is to represent these industries in general and not any particular company. Dr. Heck is employed by Lorillard Tobacco Company, Dr. Lauterbach is employed by Lauterbach & Associates, LLC, and Mr. Hamm is retired. FDA encourages all other participants to advise the

committee of any financial relationships that they may have with any firms at issue.

I'd like to remind everyone present to please turn off your cell phones. In this room, we need you to turn them off completely; otherwise, we get feedback with the microphones, and also ask you not to access the Internet while you're in this room. If you are on the phone calling in to participate, please keep your phones on mute unless you are speaking.

I would now like to identify the FDA press contacts, Michelle Bolek -- if you're here, please stand up -- and Jeffrey Ventura.

Thank you.

Introduction of Committee Members

DR. SAMET: Okay. Let me ask then the committee to introduce themselves. Dan, let's start with you, across the way.

DR. HECK: I'm Dan Heck, with the Lorillard Tobacco Company, representing the tobacco manufacturers.

DR. LAUTERBACH: John Lauterbach, Lauterbach

& Associates, representing the small business tobacco manufacturers.

MR. HAMM: Arnold Hamm, representing U.S. tobacco growers.

DR. DJORDJEVIC: Mirjana Djordjevic, with the National Cancer Institute, representing the National Institutes of Health.

MS. SHELTON: Good morning. Dana Shelton, from CDC, sitting in for Tim McAfee.

DR. DEYTON: Good morning. Lawrence Deyton, Center for Tobacco Products.

DR. ASHLEY: David Ashley, Center for Tobacco Products.

DR. HUSTEN: Corinne Husten, Center for Tobacco Products.

DR. NEZ HENDERSON: Patricia Nez Henderson, Black Hills Center for American Indian Health.

DR. HENNINGFIELD: Jack Henningfield. I'm with Pinney Associates and the Johns Hopkins University of Medicine.

DR. BENOWITZ: Neal Benowitz, University of California-San Francisco.

MS. DELEEUW: Karen DeLeeuw, Colorado Department of Public Health and Environment, representing state government.

DR. SAMET: Let's see. And on the phone I think we have Melanie.

DR. WAKEFIELD: Yes. Melanie Wakefield. I'm with the Cancer Council Victoria in Melbourne, Australia.

DR. SAMET: And, Dorothy?

DR. HATSUKAMI: Yes. I'm Dorothy Hatsukami, from the University of Minnesota.

DR. SAMET: And, Mark?

DR. CLANTON: Mark Clanton, pediatrics, public health, and oncology.

DR. SAMET: Great. So let me turn then to Corinne for your opening remarks.

Opening Remarks - Corinne Husten

DR. HUSTEN: Good morning, everyone. As you can see from the agenda, the morning session is devoted to the menthol report. As you know from previous meetings, the charge to the TPSAC is to produce a report and recommendations on the impact

of the use of menthol in cigarettes on public health, including such use among children, African Americans, Hispanics, and other racial and ethnic minorities.

As you recall, on the March 18th meeting, TPSAC produced -- and I am sorry. I'm supposed to be running the slides here. So the charge to the TPSAC.

So as you recall, for the March 18th meeting, TPSAC produced a draft report that was discussed at the meeting and then sent a report to FDA on March 23rd, 2011 that had some proposed changes in it, and those changes were from the chapter authors and the science writer. They write, "Conclusions and recommendations of the report were unchanged, but there was some addition of studies or scientific information."

In addition, TPSAC received public comments on the March 23rd report, and we'll have more comments today in the open public hearing.

So FDA is asking the committee to discuss the changes in the report and the public comments

received about the report, and determine if they wish to make any further changes to the report. And then the committee will be asked to vote on the report, which will reflect any and all changes based on discussion today. And we'll be making those changes, if there are any, in real-time here during the meeting.

So as has been mentioned before, what is the plan forward? FDA will review, and has been reviewing, the version of the report that we have, the industry prospective document and the public submissions, and FDA has also been conducting an independent review of the available science.

FDA will submit its draft review to an external peer review panel in July. And just for those of you that aren't familiar with the federal process, that's a standard government process used before dissemination of certain influential scientific information, and will make the results of both the peer review and the preliminary scientific assessment available for public comment in the Federal Register.

Then going forward, FDA will make a determination about what action or actions, if any, are warranted. There is no required deadline or timeline for FDA to make such a determination, but I should point out that any sales or distribution restrictions or product standards would be implemented through notice-and-comment rulemaking.

Are there any clarifying questions?

[No response.]

DR. SAMET: So let me just restate what we're going to do and make sure we all have a common understanding. We are revisiting the menthol report, which I know everyone had hoped we were probably done with, but here it is back. And as everyone will remember, a great deal of work was done by TPSAC at the end to complete the report and, particularly, I think, bringing it to proper editorial form.

We had input from the science writer, and I think what we will do now is have an opportunity to have additional discussion about the changes that were made as the report was brought to its status

as of March 18th, our meeting, at the time.

We've been provided with this annotated version that I think very carefully shows the changes that were made from the original version distributed for public comment in advance of the March 18th-19th meeting, so that we had the opportunity to discuss those changes.

We are going to do that now. Then we're going to have what apparently will be a brief public hearing. And then we're going to go on to look at the two specific -- at the additional specific questions, which are responses to the public comments and whether we've heard additional things that we feel need to be considered and incorporated.

We're going to look at the recommendation that was made, and then, finally, we're actually going to vote --

DR. HUSTEN: Yes.

DR. SAMET: -- just to get everyone to that. And then we have lunch, and we'll reconvene on the dissolvables in the afternoon.

So at this point, our task really is to look at what was provided to us and have a general discussion, essentially, of this annotated draft and changes that have been made.

DR. HUSTEN: Yes, the changes between what was released on the 18th and what was submitted to FDA on March 23rd.

DR. SAMET: And then just the reminder is I think Corinne provided a description of the process now that FDA has entered into, what is a standard approach to their own report and peer review of that report.

So let me ask. Are there questions for Corinne before we move on?

Dan?

DR. HECK: Yes, just a little point of clarification. Is this report subject to further modification, updating, refinement, whatever, down the road, or will this indeed close the book on this particular report?

DR. HUSTEN: This would close the book on this report. Certainly, the topic could come back

before the committee at FDA's discretion in the future, if there was no research or additional information or we had other questions that we wanted the committee to address.

DR. SAMET: Okay. Other questions? Anyone on the phone, questions?

[No response.]

Committee Discussion

DR. SAMET: Okay, good. Thanks.

Then what I'm going to suggest that we do is look at the changes and, again, as you look at the document, the extent of the changes varies and some of the changes that are here are editorial, some represented rearrangements of text, and some of this was wordsmithing, but some of it was more substantive.

I think just to maybe keep us a little bit organized, I think one thought would be to just go through, in general, chapter by chapter and see if there are any comments that anyone wants to make as we do so.

So why don't we do that just to make sure we

go through the whole report? So if everyone has this blue volume in hand, I think that would be a good way to keep us organized.

So we have a preface, with some updating of some minor details, and then the introductory chapter, which, in fact, has no annotations, so Chapter 1.

Then Chapter 2, which describes our approach to our charge, again, this is where we set out the general framework and the general approach to evidence review. Again, there were relatively few changes marked here.

Chapter 3, which was the physiological effects of menthol cigarettes --

DR. BENOWITZ: I just have one comment on page 20. There is some redacted material, and then there's sort of part of a sentence. And it seemed to me that if the bulk of the sentence is redacted, then the first part should be dropped as well, because it doesn't help. It doesn't add anything.

DR. SAMET: So you're referring to the line in red that says "Altria studies."

DR. BENOWITZ: Yes.

DR. SAMET: Yes.

DR. BENOWITZ: Because without the rest of the sentence, that's meaningless. So I suggest we just drop that.

DR. SAMET: Yes, it's a little --

Jack?

DR. HENNINGFIELD: From my perspective, the fact that they were doing the trigeminal studies, as far as I know, that's public record, and so it was useful to have that there. But there's material that can't be presented publicly. So that's how I looked at it. Even though it's awkward, if you were publishing this as a book chapter, you wouldn't do that. But for a document, I would support --

DR. SAMET: So let's ask. I think Corinne is going to speak to the principle of redaction here.

DR. HUSTEN: Well, yes, just to clarify a little bit. Obviously, in an open public hearing, if there's commercial or information that we

believe is commercial confidential, we redact it. And I realize it's a little hard to say "What do you think about this change" with part of the sentence redacted, but I think what I'm hearing you say is not to delete the sentence, but that it's hard to comment on it since you don't have it.

So, Karen, I guess we should think through if there's some way, if the committee needs to see that sentence in the meeting.

DR. SAMET: I thought Neal's point was why put in part of the sentence and then redact the rest, and I think Jack's point is sort of the opposite. It's saying that the study was done -- here we are arguing over half a sentence.

But, actually, I think the question in my mind is the more general one, which is when you do the redaction, if a study exists that is commercial confidential, why do you mention -- why is any part of it mentioned? I guess that would be my comment.

I know you have a dark room somewhere where people are doing this redaction, and perhaps --

DR. HUSTEN: I think, in general, the

principle is to redact as little as possible. So they tend to just redact the actual commercial confidential part. But I understand that it gives you sort of an odd sentence here.

But I think, for me, the question, Karen, is it's hard to comment in an open public hearing on this change since it's redacted. So if you have any --

DR. TEMPLETON-SOMERS: I'm not a redaction expert. I'm looking desperately for our FOIA people, but I don't think they're in the room.

DR. HUSTEN: No. But I guess the point is how --

DR. TEMPLETON-SOMERS: There are some people who will read an unredacted version. And so I think it's important, if the material is relevant, to leave it in. For redaction, though, we have to make public anything that we can. So that's why the partial sentence. Part of the sentence was releasable.

DR. HUSTEN: And I guess the point for the committee -- so the committee got unredacted

versions, correct?

DR. TEMPLETON-SOMERS: And the FDA will use an unredacted version.

DR. HUSTEN: And so the question for the committee is if you look at your unredacted version, is there anything about this sentence that you would want to change. And if so, okay. I think I finally was able to say that in a clear enough way.

So you have it. We can't share it with the public. If you believe this sentence needs alteration, you'll have to, I guess, tell us privately, since it'll have to stay redacted.

So the question for the committee, I guess, is do you feel like this needs to be changed over what's in the version.

DR. SAMET: Yes, Dan?

DR. HECK: Of course, not having seen what's redacted here, it's hard for me to tell. But I found myself curious. I know that Altria presented some -- in March, May, July, I don't remember when -- some briefing slides on some of the

internal research in this area.

I gather the research mentioned here must be additional studies that weren't presented publicly in that briefing.

DR. HUSTEN: In general, if we could determine that it had been published anyplace or presented in a public meeting or, in some cases, we asked the companies if they were willing to let us make it public, then -- we made every effort to make as much public as we could.

DR. SAMET: So it seems to me, in terms of a text change, no one is arguing over whether this should or should not be included, per se. It's really the more general question of the process of redaction.

So why don't we accept this? If somebody has the unredacted version available and wants to check it -- I think I have it on one or another device in my iPad, but we can look it up. But I think otherwise, there may be other examples of this, I'm forewarned. So why don't we keep going and see what else we see here.

So we're still with Chapter 3, and, again, there are some text additions and one block of text towards the end that was apparently inadvertently left out that was reinserted, but generally minor changes through Chapter 3.

If I remember right, Neal, you did a lot of this.

Phone, if you have any comments, just speak up, but otherwise, I'll take your silence as indicating that you have nothing to add.

So anything else on Chapter 3?

[No response.]

DR. SAMET: Okay. Now, to Chapter 4, Patterns of Menthol Cigarette Smoking. Again, this is one with relatively minor changes.

Patricia?

DR. NEZ HENDERSON: Yes. I don't have any -- this is our chapter and more editorial, so I agree with it.

DR. SAMET: Other thoughts about Chapter 4? Again, relatively little changes.

[No response.]

DR. SAMET: Then on to Chapter 5, marketing and consumer perception. I think everybody remembers this was a very lengthy chapter. For this one, we do have comments sent by Melanie.

DR. WAKEFIELD: So, Jon, most of the edits to this chapter are very minor. There was a larger amount of text added on page 59, which I think was contributed or suggested by Jack.

DR. SAMET: Let's see. Melanie, your proposed suggestions and edits are up, but I guess we have two slides' worth. It's the second slide. So everybody can see, there's a total of six listed.

DR. WAKEFIELD: Is that the e-mail that I sent?

DR. SAMET: Yes, it is.

DR. WAKEFIELD: Okay. Well, that's just some additions that I found in relation to the Anderson reference, which has now been published in Tobacco Control. So instead of Anderson in press, it's Anderson 2011. And I think another paper by Anderson was left out of the reference list, which

was the document, the paper on the document reviews, looking at the methodologies that had been used. So that needed to be added. And the Anderson review on menthol and smoking cessation was in the reference list and shouldn't have been.

Also, I think just a date change, which was a typo in one part of the chapter, so pretty small.

DR. SAMET: So, generally, sort of minor editorial cleanup for this one.

DR. WAKEFIELD: Yes.

DR. SAMET: And the block of text on page 59.

DR. WAKEFIELD: Yes.

DR. SAMET: Okay. Any comments about Melanie's suggestions?

[No response.]

DR. SAMET: Okay. Other comments on Chapter 5?

[No response.]

DR. SAMET: Okay. Then let's move to Chapter 6. This is Effects of Menthol Cigarettes on Initiation, Addiction and Cessation. Again,

this one with perhaps more changes than the prior chapters that we've looked at, description of the Hersey study on page 104 and a fair amount of cleanup of the text.

Comments here? Yes, Dan?

DR. HECK: Just a general comment. I continue -- and I think we've discussed this previously. I continue to have some discomfort with the reliance on the model presented by Dr. Mendez, not so much because it does comprehensively include many of the factors that might play into this equation, but I think our confidence in some of those input values for that model calculation is not really justified within the data. So I just wanted to indicate that I continue to have some discomfort with that.

We have a key reliance on a single paper, the Nonnemaker study, that drives the entire output of the model, and, to me, that's a kind of thin basis for undue reliance on the outputs of the model.

DR. SAMET: Okay. We'll come, I think,

further on to the model and how it's described.

The one comment that -- of course, one thing that the modeling approach does make clear is exactly what data we are relying on.

Dorothy?

DR. HATSUKAMI: Yes. Just going back to some of the changes that were made in this particular chapter. Just re-reading it, I didn't have any problems with the editorial changes. I think this was one of the last chapters to be reviewed, and it was during the end hours. So that's why you see a lot of the editorial changes. But there were a few corrections that needed to be made, and they're very minor.

Jon, did you want me to present those here?

DR. SAMET: Sure. Yes. That would be very appropriate. Please do.

DR. HATSUKAMI: Okay. So on page 124, this is just a clarification. It's the second paragraph from the bottom. There is a sentence in that particular paragraph that starts out "Four studies found that menthol cigarettes." In the second

line, it talks about that these studies were primarily experimental laboratory studies conducted with African American and white. It should say "female smokers." So that's just a point of clarification.

DR. SAMET: Wait one moment, Dorothy.

[Pause.]

DR. HATSUKAMI: Do you want me to --

DR. SAMET: Hang on one second. I think we're almost there.

[Pause.]

DR. SAMET: I've actually written "female" now 100 times with my pen.

[Laughter.]

DR. SAMET: Okay. Dorothy, move on.

DR. HATSUKAMI: Jon, would it be easier if we just looked at this and then I would send the comments?

DR. SAMET: I think it's best if we run through them.

DR. HATSUKAMI: Okay. So on page 144, at the bottom of the paragraph, it says -- it's the

sentence that says "and because of the large sample sizes of most." It should say "most studies." I guess "studies" was omitted.

DR. SAMET: 144. Just a moment. The electronic world is catching up with you here.

[Pause.]

DR. SAMET: Okay. Keep going.

DR. HATSUKAMI: Okay. On the next page, 145, I think there's the second paragraph, and it says "five of the eight." There was a correction that said the original text is seven. That original text was correct. It should have said "five out of seven studies."

DR. SAMET: Okay.

DR. HATSUKAMI: On page 145.

On page 146, in the second paragraph, there is a reference that is missing. It is in the middle of the second paragraph, and it starts off saying "Another trial" -- excuse me -- "Another trial recruited from the five Veterans' Administration Medical Centers." There should be a reference that -- the Foulds, et al, 2008 reference

inserted.

DR. SAMET: So you want that "Another trial recruited from five Veterans' Administration Medical Centers," and that is Foulds, et al.

DR. HATSUKAMI: Yes, Foulds, et al, 2008. That was the number, left out.

There is just one other one, so you'll be relieved to know.

DR. SAMET: Dorothy, actually, can you go back to that sentence, the one where you wanted to put Foulds, et al, and just make sure I understand what it means? "Another trial recruited from enrolling smokers who were older." And then it goes on to say "Based on a study." I'm not quite sure it follows.

DR. HATSUKAMI: You're right. It looks like something is missing from that sentence.

No, that's right. "Another trial recruited from five Veterans' Administration Centers, therefore, enrolling subjects who were older and" -- I think that -- actually, the reference should be after "therefore, enrolling subjects who

were older."

So "Another trial recruited from five Veterans' Administration Medical Centers, therefore, enrolling subjects who were older," and Foulds should be inserted there. I think that makes sense still, Jon. Okay.

DR. SAMET: And then the contrast you're implying is a study by Okuyemi?

DR. HATSUKAMI: So, basically, that's the section that describes some of the limitations of various studies that they -- some of them had a select population of subjects. So with the Cropsey study, they were female prisoners. With the VA studies, they tended to be older. And with the Okuyemi study, I think it was mostly focused on African American or just a racial population.

So discussing the select -- the population, the selected population in these studies.

DR. SAMET: Okay. And next?

DR. HATSUKAMI: And then the last one is on Table 4 on page 173. And at the very bottom, it says "follow-up rat." It should say "follow-up

rate."

DR. SAMET: Let's see. This is the bottom of page 170-which, Dorothy?

DR. HATSUKAMI: It's page 173.

DR. SAMET: I'm looking for the rat reference -- oh, the footnote. Okay. All right.

DR. HATSUKAMI: Yes.

DR. SAMET: Okay. Thank you for finding that.

DR. HATSUKAMI: Okay. I think those were my additional corrections.

DR. SAMET: Okay. Let me ask if there are others on the committee with, again, comments on this chapter, which had a number of editorial changes made to it.

DR. HATSUKAMI: Oh. Actually, Jon, I forgot one other one. I apologize for this. It was brought up by one of the tobacco companies, Lorillard, and it's on page 133. Sorry about this.

The section that says "Cessation in adults," it should read "27 studies," not 25, but 27.

DR. SAMET: Okay. All right.

Let's see. Dana, did you have --

MS. SHELTON: I was just going to point out on page 107, second paragraph, second sentence, I think we mean "2010" instead of "3010" for the submission. I think it's just an error in the date.

DR. HATSUKAMI: Hopefully, we're not reviewing this in 3010.

[Laughter.]

DR. SAMET: Got it, got it, got it. That was anticipatory in a thousand years. Okay.

Other comments? Dan?

DR. HECK: Just to kind of follow-up on Dorothy's mention from the Lorillard commentary that we had before us, there are a number kind of small errors in counts of studies and things like that represented in the Lorillard comment here.

I don't know what the best way might be to consider those for adoption. Unfortunately, the Lorillard comment was categorized kind of topically rather than by chapter, so it's a little hard to follow all of those, but there are some other

examples in there

There's an example, too, from one of the tables in this -- I think it was from the Foulds group. I'm not quite remembering where it occurred. It must have been in this chapter, where there was a misreading of the statistical significance from the data table. I can try to find that.

Now, I don't know if this would be more appropriate to talk about during the public submissions discussion or to try to ferret out some of those corrections that were pointed out.

I did see, and I was pleased to see, the clarification and the revision here between the prevalence of smoking and reference for menthol. I think the terminology now in the corrected form is much more clear on that point.

DR. SAMET: Thanks. Let me ask Corinne about this.

If there are -- and I understand that this is a fairly lengthy document that was put together quickly, and there may be things like 25 instead of

27 studies and such, and there have been a number of careful reads of this by the industry and others.

Is there a way that such comments, if viewed as corrections, can be made in a simple way?

DR. HUSTEN: Do you think you can go through it and identify a little more clearly by chapter where you think there are discrepancies? I think that's going to be the easiest.

DR. HECK: Yes. The comments that come to mind, it looks like they're on or about page 12, 13, maybe 14 of the Lorillard submission, some fairly trivial, just accounts of studies don't quite match.

DR. HUSTEN: Actually, I was wondering if you had a way of translating from that into where it is in the chapter in the document in any kind of easy way.

DR. HECK: Not before me. I have it in spreadsheet form, but I don't have that before me here. There are additional rather small errors in the main -- errors and omissions.

DR. SAMET: After the open public hearing, when we return, we're having committee discussion, the item on receiving public comments. And there are a number of public comments received on the report.

If, at that point, it were possible to perhaps take a look at these -- I've asked whether they could be put on the screen. I don't know whether that's possible or not.

Can we put up these --

DR. HATSUKAMI: I think that's a good idea.

DR. SAMET: If we could put up those pages. But why don't we wait? We'll come back to that, because we have that as a -- that's sort of our item 2 for committee discussion after the open public hearing.

DR. HUSTEN: Jonathan? One thing is, if you have it on a spreadsheet, Dan, if you could, between now and the end of the break, sort of pull that together, access it. I'm just trying to think -- it would just be easiest for the committee if it cross-referenced a bit to the actual

document.

DR. HECK: Maybe I can, as I sit here, just highlight some of the more accessible straight corrections that might be incorporated.

DR. HUSTEN: Jonathan, does that work for you?

DR. SAMET: Yes. Also, looking at just -- Dan, you're referring to the Lorillard comments specifically.

DR. HECK: Yes.

DR. SAMET: So I'm going to suggest we figure out how to get these up after the open public hearing, and, in the meantime, consider -- continue our own -- let's hold on these until we come back after the public hearing.

Okay. So we were in Chapter 5-6, right? Let me get my bearings here.

DR. NEZ HENDERSON: Jon, I have a question on page 111, on figure 8, at the top.

DR. SAMET: Okay.

DR. NEZ HENDERSON: It's very blurry. I'm just wondering is there a way to make that clearer

for readers? The printed copy is just -- I can't read it.

DR. SAMET: That sounds like that can be fixed.

Okay. Other comments on this chapter?

[No response.]

DR. SAMET: Okay. Then this will take us up -- so this takes us up to now page 188, which is Chapter 7. This is the effects of menthol on the disease risks of smoking. I think Neal and I largely authored this.

DR. BENOWITZ: This looks fine to me.

DR. SAMET: So comments here from anyone?

DR. CLANTON: This is Mark. I agree with what's there. I would make sort of a general editorial comment, which is we want to make sure that the reading audience does not misinterpret this chapter for public health impact. This is basically talking about comparative risk between menthol and non-menthol cigarettes.

I don't think we actually include that anywhere to make it clear that we're not talking

about the actual impact on lung cancer rates, for example, of menthol cigarettes. So that's just a general comment to be made, but not necessarily to be reflected in what we have here.

DR. SAMET: So, Mark, let me ask. If you look at the opening paragraph, the introduction, page 188 --

DR. CLANTON: Yes.

DR. SAMET: -- so it's fairly explicit what it's about. Are you suggesting there might be a sentence as to what it's not about?

DR. CLANTON: Absolutely. It seems kind of a clear, straightforward thing, but I have a real-life concern that people will confuse the fact that there's no real difference in the comparative risk of menthol cigarettes versus regular cigarettes, that that still might be confused with the issue that in excess of 80 percent of cigarettes smoked by African Americans are menthol cigarettes and, consequently, most of the lung cancer that African Americans get comes from those cigarettes.

So I just don't want comparative risk in any

way confused with the more important issue of actual health impact of smoking a menthol cigarette on lung cancer, for example. So I actually think it's redundant, but it's probably a still important thing to say.

DR. SAMET: So just looking at the start of that paragraph, it could say this chapter addresses the specific question of comparative risk.

DR. CLANTON: Yes. That would be helpful.

DR. SAMET: Would that be sufficient?

DR. CLANTON: Halfway there, but I'll take that.

DR. SAMET: Okay.

DR. BENOWITZ: I think we could add more to say that this chapter looks at the intrinsic risk of smoking menthol versus non-menthol cigarettes for an individual, but does not look at the impact of menthol cigarettes on the risks for populations, to just make it really clear.

DR. CLANTON: Thanks, Neal.

DR. SAMET: So what I would actually suggest is that the first sentence read "This chapter

addresses the specific question of comparative risk of menthol compared with non-menthol cigarettes," colon, and then we leave the question, because the question has been framed before. And then if you would like to add a statement that follows that question mark, then we should say "It does not address the broader issue of public health impact," which I think was your point, Mark.

DR. CLANTON: Yes. It does not address the broader public health impact of menthol cigarettes.

DR. SAMET: Okay.

DR. HECK: Just a suggestion, Mr. Chairman. Perhaps the phrasing there does not, in its entirety, address population harm or whatever, to indicate, certainly, it's part of the equation, but in and of itself, individual risk or whatever, it doesn't tell the whole story, I think.

DR. SAMET: I think Mark is just wanting to put in a warning here to the readers. Maybe another clarification. So right now, just the first sentence, at least in my rewriting of it, reads "This chapter addresses the specific question

of comparative risk of menthol compared with non-menthol cigarettes," colon, and then we give the question, because that will be consistent with the questions we phrased earlier.

Then the sentence I've added says "It does not address the broader public health impact of menthol cigarettes," which we could say, comma, "the topic of chapter" -- I guess it's Chapter 8, if I can remember. I think that would --

DR. CLANTON: I just want to make this point, not to drawn this out, but in looking through Chapter 8, we now extensively discuss, for example, the fact that African Americans have disproportionate and disparately high lung cancer rates. We actually don't talk about that there, because there is the overarching issue of cigarettes cause cancer, and it doesn't matter whether you're smoking a menthol cigarette or a regular cigarette. And African Americans had more lung cancer per 100,000 than any other population group. We don't really drill down into that. So that's why I thought it was helpful not to kind of

defer that to the general knowledge of some other part of the report, but to simply say that this issue of comparative risk does not speak completely to the larger issue of disease rates, not disease risks, but disease rates.

So, again, I don't want to draw it out, but I think it is important for the reader to understand that distinction, because we don't go in-depth into lung cancer rates and other cancer rates or even heart disease rates related to cigarette smoking in Chapter 8.

DR. SAMET: Right. So I think in the spirit of what you're looking for, without adding an awful lot -- I recognize that there are many topics that we didn't cover that might be relevant, but just to -- I think in the spirit of addressing your sort of wanting to warn the reader about what is here and versus perhaps what is to come, I just want to make sure that we're all in agreement.

Right now, I'll propose my rewording, because it's sitting in front of me.

DR. CLANTON: I thought Neal's -- Neal's

sentence I thought captured the spirit of what it is and what it isn't.

DR. SAMET: I think I've got that in the sentence I have. So we have the first sentence reading, "This chapter addresses the specific question of comparative risk of menthol compared with non-menthol cigarettes." And then at the end of the question mark would come "It does not address the broader public health of menthol cigarettes, which is covered in Chapter 8." Well, its impact, which is what's covered.

Neal and Mark, comments further?

DR. CLANTON: Well, when we get to Chapter 8, we might want to look specifically at the points where we talk about rates per 100,000 of lung cancer, and if it's there, then that's adequate.

DR. SAMET: Yes. I'm sticking with impact, in part, because that's the phrasing we've used throughout the report.

DR. CLANTON: Impact is fine, but what we're talking about, the impact is on disease and disease

rates. That's what impact is. It's not a general undefined concept.

DR. SAMET: But we've also used, for example, impact to refer to increased numbers of smokers or deferred to say lower quitting rates. So I think we'd have to think a little broader.

Neal?

DR. BENOWITZ: Well, in Chapter 8, on page 220, where we basically say that the availability of menthol cigarettes could adversely affect public health through two consequences, increasing the risk for disease caused by smoking a cigarette, which is what Chapter 7 deals with, or increasing the number of people who smoke. But we could use this text in Chapter 7, as well. I think that makes it quite clear.

DR. SAMET: We could or, simply, I've made a reference to Chapter 8 in what follows, which should cover it.

Dan?

DR. HECK: I think if, indeed, the committee does want to put in some phrasing with reference to

the disparities in lung cancer, for instance, particularly in African American males, I think it would be important for us to include the well-established fact that those excess disease burdens are also manifested in non-smokers.

So I think we don't want to over-interpret the relation of excess disease risk in black Americans to the menthol preference because that disparity is seen also in people who don't smoke.

DR. SAMET: Are you aware of lung cancer rates for African American never smokers?

DR. HECK: Yes. Yes. I think the Jamal reviews and -- well, any number of reviews, I think we see that the rate of lung cancer in non-smokers, although it's certainly lower, is also disproportionately high in African Americans, particularly males, who don't smoke.

DR. CLANTON: And at what rate?

DR. HECK: I don't know. Certainly, the rate in non-smokers is rather lower, but it's rather higher in African Americans, particularly males, than it is in equivalent white males.

DR. CLANTON: I understand. It's just that the term "high" is a relative term, and we actually have absolute numbers for African Americans who smoke and we have absolute numbers related to their lung cancer rates.

So I would be happy to look at that, but we would need to know some absolute number to understand its magnitude. So higher and/or higher probably doesn't help here, particularly since we have absolute numbers for increased risk of African American smokers and lung cancer.

DR. HECK: I believe Jamal 2009 has that number, but I will have to look at that reference. I have it on my machine.

DR. SAMET: You might do that. I'm just thinking offhand about whether there are cohorts in which actually rates of lung cancer have been measured in African American never smokers, and perhaps the only one that even comes to mind is the cohort being done by the Vanderbilt Group that we heard from on the menthol issue, but I'm not aware they have published rates.

We assembled all these data from around the world about two years ago, and I just, Dan, don't recall any data.

Mark, I do think I understand some of the spirit of what you're saying. I also want to remind you that we really did not, as a committee, review the more general problem of tobacco-caused disease in African Americans or other special populations in this report. So I think we have to be very, I think, restrictive in what we do as we look at -- take a last look at the menthol report today.

So why don't we -- we can revisit this text on Chapter 7 after we look at Chapter 8. I think any wordsmithing here needs to be relatively limited and placed within the context of data we've already gathered for this report.

So other comments on Chapter 7?

Dan?

DR. HECK: I had one, but, unfortunately, I've lost the page for the moment. There is some discussion with reference to some of the Altria

Philip Morris experimental studies, Rustemeier and perhaps Carmines, suggesting that -- and with citation of I think one of Stan Glantz's analyses -- menthol increases the particulate matter and small particulate matter in cigarette smoke.

Those authors in that paper explained that phenomenon, which basically this was an observation seen in experimental cigarettes, with very heavy loading, 18,000 parts per million of menthol. And the reason for that increased delivery of -- well, what we call particulate matter, really droplets -- is the transfer of the mass of the intact menthol in a quantitative way into the smoke.

So I think it's a little misleading to think that the statement implies that menthol increases tar. It doesn't increase the tar generated from cigarette tobacco, which is, of course, the tar of concern. Those highly loaded experimental cigarettes just transfer a lot of the excessive loads of menthol into the experimental smoke

condensate.

So I thought that section could use some clarification, lest the reader conclude that menthol results in higher tar as a general case, particularly in commercial cigarettes.

I think we saw the same sort of perhaps --

DR. SAMET: Dan, if I can interrupt, it's page 206.

DR. HECK: And I think we saw some of the same sort of misinterpretation of those findings in some of the other analyses that the FDA prepared, with a statement that menthol increases nicotine delivery in some fashion. I just think that's not a scientifically sound conclusion. There are very clear reasons why, in the experimental cigarettes that were being discussed, nicotine yield may be higher or lower, but it really wasn't due to the menthol.

DR. SAMET: Let's see. Neal, look at page 206. This is the sentence that starts "Several studies have shown that menthol." I think that one problem sentence now is it increases the

amount of tar and fine particles in cigarette smoke. So there's a definitional problem, I mean, tar referring to the filter deposited material, fine particles. There's a little bit of ambiguity here.

Dan, I think what you're trying to say is that you would like this to read "Several studies have shown that high levels of menthol in experimental cigarettes."

Is that what you're suggesting?

DR. HECK: Yes. Those high levels are transferred and captured on a glass fiber filter, but I think it would be erroneous to call -- it is tar, by definition, but it's not the kind of tar that we're concerned about generally.

There is some percentage of menthol in the condensate collected from those cigarettes.

DR. BENOWITZ: I forget the studies. Was that demonstrated or is that hypothesized that effects on the tar particles are just due to capturing more menthol?

DR. HECK: Yes. There have been chemical

analyses. And I don't recall the exact number, but the percentage of menthol in these highly loaded experimental cigarettes is in the percent rate of the captured condensate, and that's where the extra mass comes from, from the delivery of menthol.

In other ingredient studies, we have the same phenomenon. And this was discussed at some length by, I think, the Carmines paper accompanying that series from Philip Morris, because it's a problem in interpreting the study.

Do you express your histopathology findings or whatever per cigarette or per unit tar? Both can be informative, but cigarettes, particularly with high loadings of experimentally added ingredients, deliver oftentimes high levels of those ingredients into the captured condensate. But this wouldn't be a phenomenon you'd see in commercial levels of usage.

DR. BENOWITZ: As I read this paragraph, one of the concerns is not so much whether there are carcinogens in these tar particles. It really is the effects of particulates, per se. And I'm not

sure we know whether the extensive database on particulates would vary as a function of whether it's because there's more menthol in the particles or not.

This raises the concern that if you increase particulate matter -- other studies suggest that particulates are associated with some risks, like cardiovascular disease. I don't think we know what constituents of the particulates really cause cardiovascular disease.

DR. HECK: That's certainly true with particularly the environmental particulates, like diesel soot and traffic pollution. But we have to remember that these cigarette smoke droplets are droplets rather than dry ash particles in the main. There is some carbon content, certainly, but most of these experimental studies in the animal exposure, in particular, are done based on matching total particulate material in the breathing zone of the animal.

So the question generally asked, is the smoke particulate material at an equal level of

aerosol exposure more or less or equally toxic in terms of generating histopathology in the animal studies, and that was the purpose of this particular study that's described here.

DR. BENOWITZ: I think this paragraph is not definitive. It just really says that it raises concerns, and I think those concerns are still there, even though it may not be a concern if we had more data. But I still think that it does raise concerns that need to be addressed. I would favor not changing it.

DR. SAMET: So let me ask, should it say, for the point of characterizing the studies correctly, "Several studies have shown that high levels of menthol" -- I think that was one of the points that you made, Dan, earlier.

DR. HECK: Yes. And that would hold for high levels of propylene glycol or whatever the test article was. But the Carmines 2002 paper, kind of introductory paper to that series, goes into this and explains this phenomenon.

The concern I had with I think one of the

FDA white papers citing the Baker work from BAT, which was basically similar, concluding that the added ingredient increased the nicotine, it was, again, I think, a misinterpretation and one of the difficulties we have in trying to do these studies with exaggerated levels of the ingredients.

DR. SAMET: Okay. I'm going to suggest that we make that addition that I said. Also, the Rustemeier reference is not in the reference list right now. So we probably should look at that. It looks to be omitted.

DR. HECK: I'm not sure that 2001 date is correct for that. It may be 2002 on the Rustemeier.

DR. SAMET: Okay. We need to check that, but there's no reference by that author on the list.

DR. HECK: Okay. I think some of the Altria people here may know right offhand. I have it on my machine, as well.

DR. SAMET: Okay. Well, we will make sure we have that, but it's not in.

So other comments on Chapter 7?

[No response.]

DR. SAMET: Okay. Then on to Chapter 8. And here I'm going to suggest that we, since this is where we get into important findings, perhaps look at it just page-by-page to make sure we have the opportunity to discuss everything here.

So let's start with page 215. That's the first page of Chapter 8, see if there are comments here.

Here, on this page, they're all editorial, page 215. And then page 216, again, editorial changes. And 217, these are editorial changes, and this is a summary summarizing the answers to questions.

218? Okay. 219? Okay, then 220. Here we have our overall conclusions. Okay. And then at the bottom begins the section that addresses public health impact. And then to 221, where there's a paragraph that was moved. And 222 is the table. This is the results from David Mendez from the modeling.

223 -- 224, table added. Okay. And then 225, the overall recommendation that we'll come back to and some moved text and some deleted text on 225. Okay. And then 226, some more rewordings of substantial material, so if everybody could just take a look at that.

Okay. Then 227, and then topics for research, 228.

So let me ask again. This is certainly important material with some changes, and see if anybody has comments about these.

DR. CLANTON: It mostly looks like editorial cleanup.

DR. SAMET: Yes. Now, Mark, I just want to make sure that in terms of my suggested rewording in Chapter 7 in reference to public health impact in Chapter 8, that I've satisfactorily addressed the concern you raised.

Again, I take your point about the disparities for African Americans and rates of tobacco-related diseases and some other populations, but that's not a topic that we

covered, except in the most general of ways.

DR. CLANTON: Well, I think a valid comment would be, particularly with the material in that final paragraph, is that we've only described public health impact in terms of the number of people -- excess number of people who would smoke or excess deaths.

So, again, this turns out not to be about disease or smoking's impact on them, but it is what it is, which is the public health impact, as defined by more people smoking and potentially more deaths based on the model.

DR. SAMET: That's correct. Okay. Let me ask, then, before we leave this aspect of our business today, just to make sure there's no one else on the committee who has other comments on these changes.

Patricia?

DR. NEZ HENDERSON: Yes. This is just some editorial comments throughout the paper to make sure that -- in some places, particularly in Chapter 4, African American is hyphenated in the

table, so get rid of the hyphenation between African-hyphenated-Americans. And then some of the chapters, the fonts are different. So I guess these are just editorial things that we can address, but that's it.

DR. SAMET: Let me just ask Corinne.

What happens when this is finally done? Are you re-posting on the Web? Will there ever be a hard copy that you would put on your coffee table?

DR. HUSTEN: We will be posting it on the Web.

DR. SAMET: But the coffee table edition is not coming out.

DR. HUSTEN: You may have to self-publish on that one.

[Laughter.]

DR. SAMET: All right. So before we go on to the open public hearing then, anything else?

[No response.]

DR. SAMET: Okay. All right. Good. Well, thank you for the discussion. I think we have track of all these changes.

So what I would suggest we do is we go on to the open public hearing, and after that, we will take a brief break.

Open Public Hearing

DR. SAMET: Both the Food and Drug Administration, FDA, and the public believe in a transparent process for information-gathering and decision making. To ensure such transparency at the open public hearing session of the advisory committee meeting, FDA believes it is important to understand the context of an individual's presentation.

For this reason, FDA encourages you, the open public hearing speaker, at the beginning of your written or oral statement, to advise the committee of any financial relationship that you may have with the sponsor, its product, and, if known, its direct competitors.

For example, this financial information may include the sponsor's payment of your travel, lodging or other expenses in connection with your attendance at the meeting.

Likewise, FDA encourages you, at the beginning of your statement, to advise the committee if you do not have any such financial relationships. If you choose not to address this issue of financial relationships at the beginning of your statement, it will not preclude you from speaking.

The FDA and this committee place great importance in the open public hearing process. The insights and comments provided can help the agency and this committee in their consideration of the issues before them.

That said, in many instances and for many topics, there will be a variety of opinions. One of our goals today is for this open public hearing to be conducted in a fair and open way, where every participant is listened to carefully and treated with dignity, courtesy and respect. Therefore, please speak only when recognized by the chair. Thank you for your cooperation.

I think we have only one public speaker today, Jim Tozzi, from the Center for Regulatory

Effectiveness.

Mr. Tozzi, if you're ready, you have 10 minutes, not an hour.

[Laughter.]

MR. TOZZI: Thank you, Mr. Chairman.

I'm Jim Tozzi, with the Center for Regulatory Effectiveness. We're a regulatory watchdog, and we receive grants from virtually every industrial sector, including the tobacco industry.

I was pleased when I signed in today that I was given, for the first time, as the number one speaker, but the FDA staff then informed me that that should not go to my head, that I was the only speaker.

[Laughter.]

MR. TOZZI: The point that I want to make today is just a very, very basic point. The fact that the FDA and TPSAC continually, for whatever reasons, refuse not to address the adverse impacts of counterfeit tobacco, I think puts a cloud over this proceeding, because, as in the points that

I'll make, there are a lot of proceedings around the world that address this particular issue.

However, I'm heartened by the fact that FDA is going to have this peer review, which I'm going to mention in a second, and I think all stakeholders and FDA have the opportunity to examine and put as part of the record the adverse impacts associated with the use of counterfeit tobacco.

In my opinion, the crux of the issue is this. It's very difficult, I understand, for a public health body, such as TPSAC, hopefully not FDA, but possibly, to make the following statement, and a statement that I think the record demonstrates with some clarity that is supported by this very lengthy proceeding of this body is a statement that one would say "Do not smoke. But if you do, don't smoke counterfeit cigarettes."

I understand the institutional bias and the concern for a body like this to make such a statement, but I'll be interested if anyone knows of any facts that would make one suggest that that

statement is not accurate.

Now, given that, the focus of CRE from the initiation of this proceeding was to look at the adverse impacts of counterfeit tobacco. Initially, we were going to look solely at contraband, but as we got into the record, we saw very clearly that, in our mind, a huge and very extremely important issue is that associated with the health effects of these cigarettes.

Now, we felt so strongly about that that we spent considerable resources and developed an interactive public docket devoted entirely to counterfeit cigarettes, and that docket is called the "Counterfeit Cigarettes and Enforcement Forum."

It has three objectives. The first objective is to have a living compendium of what's going on in this massive world of counterfeit cigarettes. The second is to take that data and relate it to the health effects of people that smoke these types of products. And third, it is a networking forum for law enforcement agencies that use it very heavily. And we have locations around

the world that give us data, and we report on enforcement actions taken throughout the world, and law enforcement agencies use it and they come back and post some of their successes on the site.

Now, since we last met, I've had an opportunity to spend a little bit more time on counterfeit cigarettes, and I want to share with you what I think at least was an alarming event to me was that I initially, when I looked at this, it was very clear that the counterfeit market was made by organized crime around the world and large purchasing cartels. But what came out in my most recent inquiries is that the average citizen has immediate access to contraband cigarettes way beyond any mechanism that I knew existed.

In your break, just go to your computer, put into a search engine "cheap cigarettes." What will come up on that site is area after area where you can purchase counterfeit cigarettes for $20 a carton, $2 a pack.

If you compare the $2 a pack with going rates of $8 to $12, you'll see the average citizen

has now immediate access to counterfeit cigarettes. It will even tell you when you order them -- I got on, they're all around the world, they speak in any language you want -- they'll ask you the tax stamp of the state that you want. They guarantee five to seven days delivery and very minimal shipping costs.

So the point I'm making is that this is not an economist saying that this is some real far-fetched thing. Just get on the net and you'll see the impact that it has. And I'll tell you, there is not one case that asked me my age, because they know I'm so old anyway. But in most cases, you don't have any age checks on this stuff or anything. Just press a button, and they're delivered in five to seven days.

My attorneys say I can't tell you that I bought them because it's probably illegal, but I'm just telling you that you can buy them.

Now, what is the next step? We felt so strongly that this thing of counterfeit cigarettes are growing so fast, that we submitted to you a

compendium of 20 studies that we looked at that examined the health effects of these, and I'll quote, within the next three and a half minutes, just to finish up, that they're done by leading academicians, government agencies around the world, and researchers. And there is one, just for example, that's done by the Mcfarlane Burnet Institute for Medical Research and Public Health in Melbourne, Australia. It's indicative of the studies being done by other governments on the health effects of counterfeit cigarettes.

They quote-unquote, "In multivariate analyses relative to smokers of illicit tobacco, current users of illicit tobacco had significantly greater odds of beginning smoking at a younger age. Second, 6 percent greater odds of reporting below average social functioning and nearly twice the odds of reporting a measurable disability."

So the point that I'm making is that other governments are on top of this, and I humbly suggest that our government look at these effects because the research program is going

away (indiscernible).

Now, let me give you another example. If you want to look at this, you go to where the action is, and there is a lot of it in China, huge amounts of it in China. And we have now the access. We have an office in Brazil, we have Webmasters around, and we penetrate these sites into China. And you can't look at the ones in English; you've got to look at the ones in Chinese. And our Webmasters go into there, take the data out in Chinese and translate it.

Let me tell you what the Chinese government has and has hidden in back of one of their websites about these cigarettes. They say, "Many counterfeit cigarette manufacturers use mostly tobacco waste, poor, substandard tobacco, even moldy leaf tobacco. Counterfeit cigarettes and the filter paper use inferior quality products, even waste or contaminated products. Studies show that counterfeit combustion will produce a larger quantity of 3,4-benzopyrene." It goes on and on stating the negative, very negative impacts of

these cigarettes.

So where does this lead me? I think that if FDA and TPSAC cannot address, per se, these issues, they have to open the door for the public to tell people how bad these operations are. I'm not even asking you to say whether a menthol ban or anything else affects the contraband, but the mere existence of contraband cigarettes in this proceeding, I think, needs to be addressed.

If the Chinese can make statements about that, about counterfeit drugs, I most certainly don't know why a leading health agency of the world, like FDA, cannot alert the public to this. And I think the counterfeit cigarettes issue is not going away. It's going to be a cloud over and a discussion over the topic of TPSAC and the regulation of the tobacco industry, because that presence doesn't go away. The price differentials are too good and there's immediate access to kids, like I've told you.

Finally, in the next 42 seconds -- to be sure, Chairman, I will stay in my timeframe -- I

wanted to compliment the FDA on what they said early this morning. They are having a peer review of this subject. I want to emphasize to all stakeholders, that peer review is done pursuant to data quality guidelines issued by OMB under the Data Quality Act, and the peer review is subject to statutory standards and regulatory standards for completeness. Most agencies, they get to this point, they don't publicize the peer review or they duck it, and I compliment you all for standing on this very important issue.

Thank you very much.

DR. SAMET: Thank you. You did have two seconds left.

Let me ask if the committee has questions.

Jack?

DR. HENNINGFIELD: The statement that TPSAC has ignored the countervailing healthy effects of menthol ban is just, frankly, incredible. It ignores the many hours that we've spent on this topic. It ignores the considerable deliberation and public testimony, consideration of that

question-and-answer. That's all for the public record. This is including our discussion of how you would even go about providing a third of a billion cigarettes per day to 10 to 15 or more million menthol smokers by these various mechanisms. It ignores the report itself.

My conclusion is that to create these alarming conclusions, you, frankly, have to misrepresent some of the facts. You have to ignore the ongoing health disaster of menthol use. You have to ignore the potential health benefits of a menthol ban.

The report does make clear that contraband is an issue that has to be addressed. The report does make clear that this committee is not the committee with the expertise to design the mitigation strategies that would need to accompany a ban. And any ban that occurred would have to occur in the context of some approach to mitigate the problems that have been addressed and surveillance to detect the problems in a timely manner. That's all part of the law.

So my own view is that the report has thoroughly considered the topic and has proposed an approach to go forward.

DR. SAMET: That's a comment, Jack, and not a question, I think.

DR. HENNINGFIELD: That's a comment.

DR. SAMET: Okay. Other comments or questions, on the phone or from FDA?

Okay. Thank you.

Dan?

DR. HECK: I just have one question for Jim. I'm just curious about this. I think it was a recent Euromonitor report, I believe, that had a statement that 10 percent of the cigarettes consumed worldwide are contraband; in Germany, 40 percent of the cigarettes sold.

Do you have any sense in the U.S. how big the existing contraband market is or is that a knowable number?

DR. SAMET: Dan, do you mean contraband or do you mean counterfeit?

DR. HECK: I guess I mean all of the above,

counterfeit, contraband, untaxed, bootlegged, smuggled. Do you have any sense of how much of the U.S. market that pervades?

MR. TOZZI: I can give you some estimates, but I must say, they have not been replicated. The majority of the work done on contraband -- Dr. Samet, by the way, I'm talking about counterfeit cigarettes instead -- has been done in other countries.

There are people that have rejected that 20 percent here. But I've seen the numbers, but I haven't replicated them, so I cannot -- the literature, very smart. But in terms of amounts of cigarettes coming in, the DEA has a considerable amount of data on it, but we don't know how many are contraband or counterfeit. But the current study is around 20 percent, but CRE has not replicated that number.

DR. SAMET: Jack?

DR. HENNINGFIELD: I think what complicates issues and numbers like this is that a lot of that contraband are tax-free cigarettes manufactured by

the companies that are represented, that are smuggled from one state to another to avoid taxes, not cigarettes made in caves in China, as was illustrated in an earlier presentation here.

DR. SAMET: Well, I think you've highlighted the fact that this issue is not neglected in our report, and we suggested that this may need further inquiry.

So let me see if there are any other questions or comments.

[No response.]

DR. SAMET: Okay. Then if not, the open public hearing portion of this meeting is now concluded, and we will no longer take comments from the audience.

The committee will now turn its attention to address the task at hand, the careful consideration of the data before the committee, as well as the public comments.

Actually, we will turn our attention to break, and I suggest that we break until 11:00.

(Whereupon, a recess was taken.)

Committee Discussion

DR. SAMET: If everyone could please take their seats, we'll get started.

We are moving on to continue our discussion of the menthol report, and we are going to remember, at the end, to have a vote on the report.

Is everybody back on the phone? Do we have Melanie still with us?

DR. WAKEFIELD: Yes, I'm here.

DR. SAMET: Okay. And, Mark, you're back, you're here? Dorothy?

DR. HATSUKAMI: Yes.

DR. SAMET: Okay. Thanks. Thanks for hanging in. Okay.

So what I would like to do now is to go to the second item for discussion. This is the public comments. We actually have had public comments here. Public comments have come in on the posting. And I want to see if there are any changes that anyone wants to suggest or discuss in light of the public comments that we received.

Dan, just to go back to you for a moment on

the Lorillard comments, do you want to comment? My feeling is that we might be able to -- perhaps if there are minor changes, let's say numbers of studies, that kind of thing, that those could be tracked down and made, but perhaps outside the context of this discussion now.

DR. HECK: Yes. I apologize, Mr. Chairman. In trying to look through those comments, and since they aren't organized by chapter, I really had more difficulty than I thought finding the specifics.

There are some individual little comments in there. I think we'd call them some minor points that could fit into the current conversation, but I really don't think, in the interest of the time we have, that it would be useful to try to do that.

As long as those comments and the others are before the FDA for their consideration, I would not have anything else to say in detail on those.

DR. SAMET: Okay. Thanks. And we appreciate the reading of the report and, obviously, we want it to be as accurate as possible. And I think if there are changes that

need to be -- they can be pinpointed, these minor sorts of editorial changes, I think they can be sent on to make corrections, if I understand you.

Corinne?

DR. HUSTEN: Definitely, as we're considering the information, if there are some things that it's the wrong citation or inadvertently the wrong year, send that to us because as we're doing our review, obviously, we want to be reviewing accurate information. So any of that is helpful to us.

DR. SAMET: Okay. In addition to these more minor changes, looking over the public comments that were received, there were some that were more substantive, some getting at issues of framework and other matters.

I just want to make certain that the committee has reviewed those, certainly looked at them all, and see if anyone wants to bring up any matters from those comments for discussion.

On the phone?

[No response.]

DR. SAMET: Okay.

Yes, Dan?

DR. HECK: If I might, Mr. Chairman. I would encourage FDA and, indeed, the peer reviewers, yet unnamed, who will review the FDA's independent summary of this, to give fair and reasonable and equitable consideration of some of the underlying information we have before us, the industry report, the Altria report submitted last year, and then, I guess, an update to that submitted before us today for the meeting.

I think that's a very worthy and thoughtful document, and I would direct you, in particular, to the Altria submission that's before us today on these topics of initiation, dependence, cessation, these more difficult to quantify behavioral parameters.

Looking again at that Altria submission that's in the packet today, I don't think I've seen a more concise and clear analysis of that topic. If you look at anything in that report, look at those pages, pages 14 through 21. The TPSAC

report, the industry menthol report go into more detail on those, but just in a few pages there, I thought those authors did a real good job of kind of summarizing the state of the science.

DR. SAMET: Okay. Corinne?

DR. HUSTEN: Dan, I was wondering -- obviously, we are at FDA reviewing everything very carefully. I was wondering if, though, for the committee, if you would like to highlight anything in particular.

DR. HECK: Well, the authors in that PM-Altria submission explain the rationale and the state of the literature, mixed or inconclusive or whatever, on those subjects and justify their own conclusions regarding does menthol affect smoking initiation differently, concluding there that the evidence is inconsistent, recent evidence, in particular.

Their overall conclusion, the evidence is inadequate to confer the presence or absence of a causal relationship between the use of menthol in cigarettes and smoking initiation. And I think

they've laid out, again, in quite a compressed and short form, their analysis of the literature.

They conclude, also, that the evidence is suggestive of no causal relationship between the use of menthol in cigarettes and increased dependence. And, similarly -- these subjects are all intertwined, of course -- that there's no causal relationship between the use of menthol cigarettes and smoking prevalence.

So there's only a few pages summarizing the literature, and I think it's a pretty accessible way to get to at least this other independent analysis of these topics.

DR. SAMET: Okay. One moment, Jack.

I just wanted to check who is on the phone. Melanie, you're still with us?

DR. WAKEFIELD: Yes, I am.

DR. SAMET: And, Dorothy?

DR. HATSUKAMI: Yes, I am.

DR. SAMET: And, Mark, are you there?

DR. CLANTON: I'm here.

DR. SAMET: All right. Good.

Jack?

DR. HENNINGFIELD: I did review the Altria comments and the industry report again. It doesn't lead me to suggest any changes, and I don't see anything fundamentally new from what we've heard from the industry in testimony up to this point that's fundamentally different.

The Altria sections that you mentioned, in my own opinion, miss the forest by focusing on specific trees. I think on the topics of initiation, cessation, especially in youth for initiation and transition to dependence, when we have findings, they are generally in the direction of increased initiation, increased transition to dependence.

The general conclusion that there's no disproportionate effect of menthol on any demographic group flies in the face of all of the evidence that we've seen in toto. So I have looked at it. I don't see anything that would lead me to change anything that's in the TPSAC report.

DR. SAMET: Okay. Other comments? I might

make one, in part, because the framework that we used is important, and there were a number of comments, I think largely from the industry, about the framework we used and the concept of equipoise.

That term is a well established term, I think often used particularly in the clinical trials literature for where the evidence stands. It was not unique or particular to the report on Veterans' compensation, but was used there because it was thought to be a reasonable point to bring to the attention of decision makers.

I think the logic was the same in our committee's using equipoise and noting where the evidence stands, because in the end, presumably, this or other reports will become part of the basis for decision making, and there are further comments on the strength of the evidence as it moves into higher categories.

I'm quite familiar with the Surgeon General's criteria, having been the senior scientific editor for the 2004 report, and I think as a general comment there, there are gradations of

the strength of evidence that are within the categories given. They are simply not linked to a particular point where the strengths of the evidence or the extent of evidence as weighed against uncertainty is viewed as reaching a point of equipoise or not.

So I think the idea of categorization, the strength of evidence is similar, one set of categories, those used in the menthol report, simply have an anchoring point. And it put the burden on us as identifying where the evidence stood as we tried to look at what we know versus what we don't know.

So I think it's important to note that, because I think our conceptual basis for classifying the evidence is laid out in Chapter 1, or Chapter 2, and some of these connections were made. But because there was so much response to this point, I just wanted to add this to our discussion.

Neal?

DR. BENOWITZ: I'd like to make one comment

on one set of criticisms of the report which had to do with looking at analyses by either all menthol smokers, whites and blacks together, or by looking at state-by-state differences, just to make the point that smoking behavior is so complicated that it really -- we're looking at a combination of effects of products and effects of marketing and effects of culture, and you can't separate those out.

So the fact that you might find an effect in African Americans, but you don't find it in whites, to me, does not argue against any causal relationship. Really, the marketing and the culture of menthol use among African Americans is so different than whites. And I really think that that argument, that because you see it in one group but not another means that there's no effect, is not a viable argument.

The second kind of argument was made that if you look at the percent of menthol use versus the prevalence of smoking in different states, that it's not strongly correlated. Again, states are so

different in terms of local public health policies involving smoking, the culture of smoking from state to state. I really don't think that is a valid comparison to look at that. One really has to look at within states and within a given public health environment and within a given culture.

So there were a number of arguments like that made, and I think one really needs to look at the combination of the product and the marketing and cultural environments.

DR. SAMET: Okay. Any other comments here? Anyone on the phone, just to make sure you're not forgotten? Again, we're still with sort of item 2 on our agenda for 11:00 to 12:00.

[No response.]

DR. SAMET: Okay. Then let's go on to item 3, and we're going to take this on, and because of its importance, go around the table and talk about this individually.

So item 3 says in the menthol report, TPSAC made the following recommendation: removal of menthol cigarettes from the marketplace would

benefit public health in the United States. And our charge as we go around to discuss this is to state whether we agree or disagree and provide a basis for that agreement or disagreement.

So I think what we'll do is I'll start and state that I do agree with this statement. And, again, much of this comes from how we put the evidence together in our overall framework and model for looking at those aspects of the process leading from experimentation to initiation, to eventual causation of disease by smoking, looking at those steps and identifying where the availability of menthol compared to non-menthol cigarettes -- remember our so-called counterfactual which underlies this discussion.

We identified several points where the evidence would suggest that, in fact, there was an adverse impact on public health. And the model, the work done by David Mendez, using parameters based on the literature, acknowledging that there's uncertainty, there was always uncertainty, still gave us a quantification of that public health

impact, suggesting that indeed it was substantial and adverse.

So that is my reasoning for agreeing with the recommendation that was made.

So I think what we'll do first is go next to Karen.

MS. DELEEUW: I would also agree with the recommendation, and, certainly, Dr. Mendez's population dynamic model played an important role in coming to that conclusion. And looking even at the low estimates, the smoking attributable deaths and deaths averted if menthol is banned was, I think, pretty compelling.

I continue to have concerns over the high menthol cigarette use among minority youth and the continuing rise of menthol cigarettes among adolescents and youths. And I also found the information presented by Anne Hartman from the 2010 tobacco use supplement of the current population survey, the question, if menthol cigarettes were no longer sold and asking that to people who smoked menthol, and that response being 39 percent of

those respondents said they would quit, and among the African American population, 47 percent said they would quit.

So those are some of my reasons.

DR. SAMET: Neal?

DR. BENOWITZ: I would support the conclusions, and I'll make a few comments in response mostly to the criticisms. First, I have to say that it is true that the data are not as extensive as we would like. That's always the case, and the issue here, I think, is how long you wait for more and more data. If we wait five years, we'll have more data, if we wait 10 years. But there's always a potential public health cost of waiting, and we need to weigh the decisions that we think we can make pretty well with existing data versus waiting more and more years and more and more costs of health.

So I think that's part of the problem. We would always have liked to see better data and more data, more extensive data, especially longitudinal data, but we basically looked at what we had

available.

There were some criticisms about the biological plausibility in terms of specific receptors or, rather, how much desensitization there is, but I think it's really clear that menthol has got effects. People who smoke menthol characterizing cigarettes like them. They like the menthol taste. Menthol reduces the harshness.

No matter what you say about it, there is something about menthol which makes it more attractive to some smokers and they like it and they smoke, in part, because of that. So no matter what you say, there's a clear biological plausibility that menthol is responsible for some people smoking who would not otherwise smoke.

The key issue in terms of the model, I think it was the Nonnemaker study. That's the one longitudinal study that really looks at the effects of early use of menthol on persistence of smoking, which is a really key issue. We had that one study. It was not the biggest study, it was not the most representative study, but that study

raises very serious concerns that there is an issue that starting with menthol means that you are less likely to smoke later on. And given that those are the data we have, to me, I think those were very important data.

The data on level of dependence, there doesn't seem to be convincing data for adults. The data for adolescents do seem more compelling. I think one needs to look at the trajectory of developing dependence, and if menthol is operating in some of the ways that it might be, what it might do is accelerate the development of dependence, which would be seen in adolescents, but not necessarily in adults. So the fact that you see it one group but not the other is not bothersome to me. I think it makes sense.

So I think, in conclusion, the tobacco industry documents themselves acknowledge that if some people really like menthol, they may smoke those cigarettes and they choose it just like they choose any other flavor. And if menthol was not there, fewer people would smoke cigarettes. That's

an important fact.

Menthol is not intrinsic in cigarettes and if menthol makes more people smoke, if it makes cigarettes more addictive for some people, especially if it's combined with marketing, that is a serious public health problem.

So in balance, I think that while there are some mixed data, while our report is not as complete as it might have been if we had more time, that the data are sufficient for me to support the conclusion that it's a public health problem.

DR. SAMET: Thank you, Neal. I just want to make one correction. In describing the results of the Nonnemaker study, you had a momentary misspeak when you said menthol cigarettes would make it less likely. I think you meant to say more likely, just to correct that.

DR. BENOWITZ: Yes.

DR. SAMET: Okay. Jack?

DR. HENNINGFIELD: I also support conclusion 3. On Neal's comments, I agree that on the addiction issue, menthol probably contributes

to addiction by many different mechanisms, making it easier to self-administer the nicotine in addicting doses, serving as what we call a discriminative stimulus in a condition of re-enforcer, its role in marketing, perceptions that it may contribute to less hazardous cigarettes.

All of these things are hard to disentangle. So when you look at just one, you're missing the forest for the tree.

Frankly, indeed, the main concern of the industry is loss of market. And let's be clear, loss of market will result from more people quitting, from fewer young people starting, from fewer people who do try smoking making the transition to addiction. That's good for public health. That's what this is all about, and that translates to fewer premature deaths and disease and disability. That's what this is about. So I think we can't forget that. That's real.

Furthermore, in terms of demographics and populations, youth are disproportionately hurt. African Americans and other minorities are

disproportionately hurt and will be helped.

So those are the main benefits. I think the damages and benefits are clear. There are concerns that are some theoretical and some plausible, like contraband, that need to be addressed, that I believe can be addressed. But those are matters that can be worked out through the public comment and rulemaking process.

DR. SAMET: Good. Thank you. Patricia?

DR. NEZ HENDERSON: I agree with the recommendation and, like my colleagues, the evidence is strongly there.

I go back to our first meeting, or I think it was on the second day when we were discussing -- there was a presentation on the demographics. And then after that, there was a series of presentations that were made by the industry. And the question was asked, do you target African American communities, and the person responded from the industry "no."

For me, that really stood out and as we began to get more information and more data, it

clearly shows that there was targeted marketing and why there is increased preference for menthol smokers among African Americans.

So all this came together at the end as we were putting the document together, that there is targeted marketing. There are definitely higher rates of smoking of menthol cigarettes among African Americans, which is, for me, very disturbing. And as we look at the data, the industry has done a great job in that. And it's -- so, therefore, I agree with the statement, and no comments.

DR. SAMET: Thank you. Let's go to the phone. Melanie?

DR. WAKEFIELD: Yes. I also agree with the recommendation. For me, overall, I've been struck by the weight of evidence or the complementarity of evidence from different fields of inquiry that we've looked at.

I suppose, given my background in psychology and communications and marketing, I found particularly persuasive the evidence that marketing

of menthol cigarettes has targeted the young and African Americans. And it is absolutely no accident that these are exactly the two groups that have high proportions of smokers who smoke menthol.

I also thought there was strong evidence that some of the early menthol marketing messages promoted explicit health benefits. As time has gone by, this has given way to sort of more the use of color and imagery and descriptive terms and so forth. And we see from the literature and the evidence that consumers mistakenly interpret these queues to imply reduced harm.

I think some of the literature on perceived harm was conflicting. It wasn't straightforward. But I think when you really weigh the studies and take account of the methods used and pay most attention to the studies that use the most appropriate research designs and methods of questioning, you see that there is strong evidence that consumers have beliefs about implicit health benefits of menthol cigarettes. And that's especially the case amongst African Americans.

But one of the things that has really impressed me about the literature is that the public health problem is not just due to marketing. It's also about the menthol product itself. And I had not read much about menthol before I embarked upon this exercise, and I was most persuaded by the careful analysis of the evidence in Chapter 6, which really shows that the harm caused by menthol cigarettes is also related to the gateway or induction role in providing an easier passage into regular smoking and progression towards addiction among young people.

It seemed to me that this evidence came from multiple lines of inquiry about issues of uptake and addiction, and it included a well conducted cohort study. And the conclusion relating to uptake and addiction was very much complemented I think by the evidence that addition of menthol, through its cooling properties, likely reduces the perception of harshness or throat grab when cigarettes are inhaled. And for me, that provides a pathway through which menthol could facilitate

progression towards regular smoking in the young.

I also appreciated the careful analysis of the literature and the evidence on cessation and the finding that menthol reduces the likelihood of quitting, particularly in African Americans. And sifting through those studies was complicated, but I do think that a terrific job was done there by giving weight to the larger population surveys that had the largest sample sizes and the widest age ranges and enabled a good comparison of quit rates in various racial and ethnic groups.

Then I think coming back to the marketing and consumer perception, again, just the fact that we did find in the consumer perception literature that African Americans are particularly the ones that have beliefs about implicit health benefits of menthol cigarettes. So these misconceptions could be one of the factors that undermines their success in quitting.

So I think, in summary, really, for me, it's the cohesiveness, I think, of the evidence across these different areas of literature that we've

looked at. That is the most persuasive thing to me.

DR. SAMET: Okay. Thank you. Dorothy?

DR. HATSUKAMI: Well, I don't really have very much to add to what has already been said. But I, too, thought the conversion of evidence was also very persuasive in terms of agreeing with the recommendation that we have made.

So I think some of the additional information that wasn't spoken about was the finding that there does seem to be a higher proportion of menthol cigarette smoking among youth smokers compared to the adult smokers, and the fact that even among the youth smokers, you see a higher proportion of menthol cigarette smoking compared to the older adolescent population.

I think there was really quite a lot of consistency in those findings, as described in Chapter 6 and in Table 1. And this type of gradient isn't necessarily seen with non-menthol smokers, and that was described in a paper by Giovino in 2004.

So this gradient is of real particular concern, the fact that there is a significant number of our youth smokers smoking menthol cigarettes, because that, of course, is the particular age where people may begin smoking.

So I think that was very compelling information, as well as the real concern, as Karen had pointed out, that there is a trend upward towards adolescent smokers smoking menthol cigarettes, whereas you don't see that necessarily with the non-menthol cigarette products. And the upward trend may not necessarily be seen in such products, such brands such as Newport, but you do see that upward trend in some of the other brands, such as the Marlboro Menthol or the Camel Menthol cigarettes. So that again is of real concern.

I know that the tobacco companies have talked about the fact that the prevalence of smoking is reducing among adolescent smokers. Yet, one of the analyses that was conducted by Giovino had demonstrated that the slope is different, that you see a steeper slope among the non-menthol

adolescent smokers compared to the adolescent menthol smokers. So I think that that is also of concern.

I know that there has been a lot of criticism regarding the Nonnemaker article that our TPSAC committee had relied upon. But as Neal had said, this was really the only article that was available that carefully looked at this issue, and it was an article that TPSAC committee members looked at. And in spite of its limitations, we believed that it was very persuasive in showing that the initiation with menthol cigarettes may increase the risk for more established smoking, as well as dependence.

I think although there was no evidence to support that adults were more dependent on menthol cigarettes compared to adults smoking non-menthol cigarettes, I think the evidence in adolescents was very persuasive.

The majority of the studies that we looked at had been published, they were scientifically sound, and they used various indicators of

dependence, and they were conducted in a large population of adolescents.

I don't think -- in looking at some of the documents the tobacco companies had submitted, the ones by Lorillard, as well as Altria, as well as the one in the big red book, I don't think they paid enough attention to that particular topic.

So with regard to cessation, I agree with Melanie that I think that there is very strong, sound evidence in indicating that the African American population, in particular, experience less cessation success if they smoke menthol versus non-menthol cigarettes.

I have to admit that this is a difficult body of literature review, because there are so many different types of studies. Some of these studies have non-representative population of smokers, some of them have small sample size when you're examining sub-population of smokers, and they also have term criteria of cessation, and there were a number of other issues, as well.

I believe that in the Lorillard document,

they indicated that cessation should be defined as six months or longer, but I'm not really sure whether that's really the best criteria to use in evaluating this body of literature.

So I think, actually, the most informative studies on this issue are the national surveys and, as Melanie had pointed out, it's because they're the most representative sample of smokers.

If you do take a look at the literature, as I had mentioned, some of the samples looked at female prisoners, or they were older samples, or they had chronic obstructive lung disease. So I think the surveys are the ones to really focus on to examine the role of menthol on cessation.

So in light of the data from the national surveys that assessed the effects of menthol on different populations of smokers, I was really struck by the consistency of results when independent investigators analyzed the same survey, but also the consistency of results across surveys, particularly with NHIS and the CPS test, the survey data.

It was noted by one of the documents that we had forgotten to mention the Mendiondo report in 2010. So I did take a look at that article, and I must have inadvertently missed it, because -- we may have missed it because the title wasn't necessarily reflective of cessation.

I analyzed the data and that, too, that database, too, also showed that there was a lower quit ratio among the black menthol versus the non-menthol smokers, and there were no differences in the whites or in Hispanics.

So, actually, if you take a look at the survey study, about six out of the eight national surveys, they support the finding that black -- the African American population -- do suffer lower -- experience lower rates of cessation if they smoke menthol. Now, most of these studies use the ratio of former to current smokers, but there was one study that did look at a six months period of cessation, and they also found similar results.

The considerable concern over the lower cessation rate among African Americans is

underscored, I think, by the high prevalence of use of menthol cigarettes among this population, the marketing that has been targeted toward this population, and the issues of health disparities associated with this population.

So, in summary, I believe that the rate of public health harm of menthol cigarettes is among our children and the minority population. And I think that there is strong evidence to support the conclusion that the availability of menthol increases the likelihood to start using cigarettes among adolescents and decreases the likelihood of stop using, particularly among African Americans.

DR. SAMET: Okay. Thanks, Dorothy.

Just to make clear, actually, when you began, you didn't state whether you agreed or disagreed with the recommendation. So I think after that long discussion, I think you agree.

DR. HATSUKAMI: Yes. I embedded my agreement in my long discourse. So, yes. Yes, I do agree.

DR. SAMET: Okay. Thank you. Mark?

DR. CLANTON: I certainly agree with the conclusion of the report and recommendation of the report. But I think, more importantly, by looking carefully at the report, the chapters and the data that was reviewed and how we weighed the quality of the evidence and pushed it through the equipoise model, I think the report actually supports the conclusion of the report quite nicely. And I think that's a small point to make, but I think it's relevant, which is the report actually nicely supports our conclusion.

It's very clear that everyone has really made the major points, but I would just emphasize briefly on a few of them. Dorothy did a very nice job focusing on something that I wasn't aware of until I took a look at the studies and data, which is that menthol has and plays a very large role in smoking initiation in youth.

Youths prefer menthol and whether it's related to the careful calibration of menthol levels and the effect that has on lessening irritation or improving the smoking experience,

however that works out, it's very clear youth initiators prefer menthol cigarettes.

Beyond use initiators, there is the use of persistence. And, again, back to African Americans and potentially some other groups, like Hawaiian Pacific Islanders, they persist when they initiate with menthol and, in fact, continue smoking and become lifelong smokers. In fact, there is very little switching between those two persist in smoking menthol cigarettes and those who might switch to non-menthol cigarettes, meaning that they maintain that preference.

On the issue of preference, there was a small thing that came up, but I think it could become a major area of research, which is this issue that has been made clear by both the industry and by our own data, which is there is a preference among youth, youth initiators and certain ethnic groups for menthol, and it's going to be important to answer the question why is that so.

So we did talk very briefly about this issue of a genetic distribution of super-tasters, those

who detect the bitterness at fairly low levels. And, again, more research in this area may help us understand why groups prefer mentholated cigarettes versus non-mentholated cigarettes.

Lastly -- actually, two last points -- the population dynamics model from David Mendez I think was very important. I simply feel that there will be more studies, hopefully, replicating the Nonnemaker study. And, again, we can run it through that model, and I think that model provides a very nice quantitative estimate of what happens because of the existence of menthol in mentholated cigarettes.

The counterfactual, by the way, I think is pretty important. It looks like we have about 34 percent of the population who smoke, who smoke menthol. In fact, if there were no menthol, there would be no menthol-related adolescent smoking initiation. There would not be menthol persistence in certain groups, like African Americans, Hawaiian Pacific Islanders, maybe even some Philippine and Asian groups. That persistence wouldn't exist.

And, in fact, in the counterfactual, we would have a considerably lower smoking rate and certainly a lower health impact as a result of lower initiation and persistence.

So those are the things that were compelling to me. But I want to make the point, I think the overall report, taken collectively, all the diverse topics, it supports very nicely the conclusion.

DR. SAMET: Okay. Thank you.

Then what I'm going to do is go to our industry representatives and then our agency representatives. Dan?

DR. HECK: Well, I'm not privileged to vote on this matter, but I'll be pleased to share my impressions on this topic.

My opinions on this are largely represented in the industry report. I do not agree that menthol cigarettes have a disproportionate impact on the public health relative to non-menthol cigarettes.

I think there are some points of agreement between myself and the companies I represent and

this committee. I think that there's broad agreement on the reality that menthol cigarettes do not appear to be measurably more toxic, more risky to the individual than do non-menthol cigarettes, based on a pretty good sized body of epidemiology evidence. There does not appear to be any compelling evidence from experimental toxicology that menthol cigarettes are more harmful, as it can be measured in animal and in vitro assays.

We have evidence from a good number of biomarker studies, including the recent one from Dr. Caraballo at the CDC demonstrating that menthol smokers do not have higher exposures generally to toxic smoke constituents.

So the question, as we work through it here, does not seem -- seems to have drifted a bit from the narrow question of are menthol cigarettes more risky -- they appear not to be -- to these behavioral aspects, smoking initiation, dependence, cessation.

I certainly agree with some of the things Neal said. These complex human behaviors are

indeed very complex and very much subject to effects of social situations, socioeconomic condition, et cetera. We've heard mention of a number of studies, a good number of studies demonstrating that besides the health inequities and social inequities, there are associations with difficult social situations and difficulty in quitting or in initiating smoking, that kind of thing.

So I think that makes it all the more important that we be cautious in taking one element of that complex milieu of circumstances, that is, a preference for menthol cigarettes that is indeed high in the African American community and high in certain age groups, and take that and develop a causal inference from that that menthol is causing these complex behaviors, because we have any number of studies from the social sciences and others that demonstrate a very potent association with a number of factors, poverty, stress, et cetera, and smoking.

We've heard mention a couple times of the

telephone survey study that was presented here to the committee where smokers and menthol smokers indicated a likelihood that they would quit if the cigarettes they prefer weren't available.

We've seen a lot of studies over the years with smokers' stated intentions to quit. Few of those are less than 50 percent of that population and some broach 80-90 percent. So a stated intention to quit, in general or given a certain circumstance, is not unusual, and I don't think it's unique to this situation here.

We've heard mentioned the fact that smoking is indeed declining. Cigarette sales are in decline. Menthol cigarette sales are in decline, as well, albeit at a modestly lower rate. I don't think that we have a sufficient compelling body of evidence from soundly designed studies in the behavioral areas that is adequate to support a sound, defensible, regulatory, science policy that treats menthol cigarettes any differently than non-menthol cigarettes.

DR. SAMET: Thank you. And just to point

out that, in fact, this is not around voting. A vote will come, but it's on the report.

John?

DR. LAUTERBACH: I also object to the report, though, for perhaps some different reasons. I'm very concerned about the science base used in the report. Journal articles, which we pointed out, had defects in there and in the methodology are still in there without any comment to that effect.

There's a lot of sensory data that came before this committee; yet, no one asked whether or not that sensory data was conducted under conditions that ensures validity. Yes, you can do very good sensory studies on cigarette products, as most consumer products, but you have to be very careful in how you control those studies in terms of making sure that they're accurate.

The committee apparently also relied upon these studies from the University of California, San Francisco. I can assure you -- and I've dealt with the legacy library documents since

1998 -- that so much of the important material was missed. The committee got a very short piece that is truly not representative of the menthol literature that's in the legacy documents.

Thirdly, the journal articles that appear to be cited appear to come from one sort of -- type of section of the scientific journals. The journals appear to be coming from -- or articles appear to come from essentially anti-tobacco journals. They're not across the entire spectrum of regulatory journals. So, again, that raises the question about how well these journals have been -- the articles have been peer reviewed.

Fourth, we still have the issue, as Mr. Tozzi presented again this morning, about alternate sources of mentholated product either coming in from overseas, coming in from other places, things unknown.

That's my comments.

DR. SAMET: Thank you. Arnold?

MR. HAMM: Thank you. Let me preface my comments, though, with a fact that I don't

particularly like the way the question is posed. It's kind of like being asked to answer the question, do you still beat your wife, either yes or no. It's kind of hard to answer the question.

I can certainly appreciate all the time and effort that went into the report; however, I can't support the overall conclusion. I have several reasons for this.

I don't feel the statutory requirements have been fully addressed that concern contraband and illicit trade. I'm not fully convinced the pertinent federal agencies were consulted. We did hear from an association, the National Association of Attorneys General, and they essentially just spoke to a tax avoidance issue, not contraband or counterfeit cigarettes.

Personally, I feel there's been too much reliance put on the legacy tobacco documents. I don't view this approach as particularly scientific nor particularly relevant to today's tobacco industry.

While I can appreciate Dr. Mendez's model, I

think maybe too much reliance was put on it. Apparently, there's only a very limited amount of research put into the input data on this. And then after discussing Dr. Mendez's model, I just think there are too many moving parts, and it's yet to be proven or validated.

Finally, some of the studies and reports that we've seen were unpublished and probably not peer reviewed. They may have been peer reviewed since. That's my comment.

DR. SAMET: Thank you. NCI, Mirjana?

DR. DJORDJEVIC: I need to make a disclaimer that NCI has not taken an official position regarding this issue, but I can present my personal views. I support all conclusions and recommendations in this report, and I'm in agreement with all comments which were given here today by the members of TPSAC. I don't need to go again over them.

Specifically, it is compelling evidence about menthol being used as a starter product among youth; that there has been exercised targeted

marketing to specific populations; and, specifically, among African Americans, prevalence of 70 to 80 percent of smoking menthol cigarettes, which results in adverse health effects.

It was compelling modeling by Dr. Mendez about the impact of removing menthol cigarettes on the public health.

DR. SAMET: Thank you. Then Dana from CDC.

MS. SHELTON: As Mirjana did, I have to do for CDC. CDC has not taken an official position on this recommendation or the conclusions of the report.

For me, as an individual professional in the tobacco control field, I think when you look at the kind of -- the body of evidence that's included in the report, any aspect of a product that would influence or increase use of tobacco products is of concern.

I think the report, there's a fair amount of evidence that suggests that menthol may indeed have influenced rates, particularly among adolescents and younger adolescents. I, as a professional,

find that very concerning. And, again, as I said, CDC has not taken an official position on the report.

DR. SAMET: Okay. I think as a last comment, because there's been so much comment about what we said and what we didn't say, we didn't use the word "ban." The recommendation reads "removal." And others have commented on the format of this overall recommendation. I would say, I would just remind everyone that beneath this, the text that follows says "The Act offers a variety of mechanisms for FDA to consider if it concludes that it should pursue this recommendation. At this time, TPSAC has no specific suggestions for follow-up by FDA to this recommendation."

Again, I just want to remind everyone that we did say that, that we are the Tobacco Products Scientific Advisory Committee; that in making this recommendation and addressing the question of adverse public health impact, we do not explore one or another potential scenario that might be pursued with regard to addressing menthol cigarettes.

So I just wanted, again, because there has been substantial discussion following our wording, just to remind everyone of the wording that explains the form of our recommendation.

Having done that, I think we've had a thorough discussion and airing of this recommendation.

Now, what we are going to do now is take a vote. The voting question is, is this menthol report reflecting any and all changes made during today's meeting, your report, and recommendation to FDA on the public health impact of menthol in cigarettes?

So that is the question. And we're going to use an electronic voting system for the meeting, except that those who are on the phone are going to send their votes by e-mail, I guess, to Karen.

Is that correct? To Tom Graham. Okay. And Mark will vote verbally last.

So those of you who are here have three voting buttons on your microphone, yes, no and abstain, clearly labeled. So once we begin the

vote, press the button that corresponds to your vote.

After everyone has completed their vote, the local votes will be locked in. At that time, we ask that the three voting TPSAC members who are participating electronically submit their vote by e-mail or marks.

We'll enter these votes into the program. The final vote result will then be displayed on the screen. I will read the vote from the screen into the record. Next, we will go around the table and each individual who voted will state their name and vote into the record, as well as the reason why they voted as they did, hopefully keeping that explanation brief.

All right. We will now begin the voting process for question number 4. Let's hope we get this right. Please press the button on your microphone that corresponds to your vote. Press now.

[Voting.]

DR. HUSTEN: While they're tallying, if I

could just clarify, especially for folks who maybe are less familiar with the process. In the voting process, the industry representatives do not vote. Again, there may be people in the audience who haven't been here. And ex officio's do not vote either. So I wanted to just clarify procedurally.

DR. SAMET: Okay. Good. Thank you.

Then I think all can see the vote here. There are eight yeses and zero nos.

So now that the vote is complete, we will go around the table and also to the telephone and have everyone who voted state their name, their vote, and the reason they voted as they did in the record.

Remember, what we are voting on is this question, not the one we just went through with the recommendation, but this is, is this menthol report reflecting any and all changes made, during today's meeting, your report and recommendation to FDA on the public health impact of menthol in cigarettes?

So to start with what I hope will be a model of brevity, my name is Jon Samet and I voted yes.

This report has been developed by TPSAC over 10 and now 11 meetings. It reflects the work of the committee. And I think I will only say that I think we stand by this work and our findings and recommendations to FDA.

Karen?

MS. DELEEUW: My name is Karen DeLeeuw. And, yes, this is my report, and I participated fully in committee proceedings and participated on the writing groups, and, again, fully support the recommendations in the record.

DR. SAMET: Neal?

DR. BENOWITZ: Neal Benowitz. I vote yes. And while it would be nice to have much more data and much more time to prepare the report, I think our committee looked at the available data and the data as a whole were very compelling.

DR. SAMET: Okay. Thank you.

Jack?

DR. HENNINGFIELD: I'm Jack Henningfield. The report does represent my report and recommendations, and my reason is that menthol

cigarette design, manufacture and marketing are a cause of great harm to public health. Removal of menthol has a potential to contribute greatly to reduced smoking and disease. I hope FDA acts expeditiously on the obvious implications of the report.

DR. SAMET: Thank you.

Patricia?

DR. NEZ HENDERSON: My name is Patricia Nez Henderson. And, yes, this is the report and the recommendation to the FDA. And the reason is that it reflects the work that we have done, and I stand by the findings of this report.

DR. SAMET: Thank you.

To the phone. Melanie?

DR. WAKEFIELD: Yes. This is Melanie Wakefield, and I voted yes. I confirm that I participated in deliberations on the report and in the writing group, and I stand by the recommendations. And I also hope that the FDA acts on it in a timely fashion. Thank you.

DR. SAMET: Thank you.

Dorothy?

DR. HATSUKAMI: This is Dorothy Hatsukami, and I voted yes on the report. And I had contributed to the writing of the report, as well as the deliberations, and I believe that there is sufficient evidence to demonstrate the public health harm of menthol cigarettes.

DR. SAMET: Thank you. Mark?

DR. CLANTON: My name is Mark Clanton. I was a member of the writing group, and I say, yes, this is my report and does reflect the deliberations and analysis and conclusion of the writing group and discussions involved with testimony, et cetera. So I vote yes and agree with the product of the report.

DR. SAMET: Thank you. I think we have completed the vote. I understand our next duty, I thought, was lunch, but, Corinne?

DR. HUSTEN: I just wanted to thank the committee, everyone, including our non-voting members, for their hard work over the past little more than a year. And I know that a lot of time

and effort went into this report from everyone and FDA truly appreciates how much effort did go into producing the report and finding the evidence and synthesizing it. And as stated, we're looking at all of the information that we received from all parties very carefully, and we'll be taking all of that into account. But I really wanted to thank everybody for what I know was a large and intensive amount of work.

DR. SAMET: Okay. Thank you. And we are, speaking for the committee, glad that that work is over.

[Laughter.]

DR. HUSTEN: And now you can move on to the next topic.

Adjournment

DR. SAMET: Yes. Now we can move on to the next topic. Okay. Thanks. Thanks for the reminder. Before we do that, we'll break for lunch and let's try -- we will reconvene at 1:00.

(Whereupon, at 12:12 p.m., the morning session was adjourned.)